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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/532,297	08/24/2005	Joseph Alexander Lasky	ON/4-32744A	1063

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CORPORATE INTELLECTUAL PROPERTY
ONE HEALTH PLAZA 104/3
EAST HANOVER, NJ 07936-1080

EXAMINER	
THOMAS, TIMOTHY P	
ART UNIT	**PAPER NUMBER**
1628	

MAIL DATE	DELIVERY MODE
10/19/2009	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/532,297	LASKY, JOSEPH ALEXANDER	
	Examiner	Art Unit	
	TIMOTHY P. THOMAS	1628	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *11 August 2009*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *2,5,7,10 and 11* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *2,5,7,10 and 11* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

1. A request for continued examination under 37 CFR 1.114 was filed in this application after appeal to the Board of Patent Appeals and Interferences, but prior to a decision on the appeal. Since this application is eligible for continued examination under 37 CFR 1.114 and the fee set forth in 37 CFR 1.17(e) has been timely paid, the appeal has been withdrawn pursuant to 37 CFR 1.114 and prosecution in this application has been reopened pursuant to 37 CFR 1.114. Applicant's submissions filed on 5/12/2009 and 8/11/2009 have been entered.

Response to Arguments

2. Applicants' arguments, filed 5/12/2009, have been fully considered but they are not deemed to be persuasive. Rejections and/or objections not reiterated from previous office actions are hereby withdrawn. The following rejections and/or objections are either reiterated or newly applied. They constitute the complete set presently being applied to the instant application.

Applicant argues that the present final rejection is premature, and requests withdrawal of the finality of the rejection; that claim 4 was present in the application at the time that the prior art rejection was made and there was no indication that Applicant intended to abandon the subject matter; that every claim from which claim 4 could have properly depended related to and required the administration of imatinib to a patient for the treatment of pulmonary hypertension; that applicant understood not including claim 4 in the art rejection to mean that claim 4 was patentable over the prior art and that the

art rejection could be overcome by limiting the main claim to the scope set forth in claim 4. This argument is not persuasive. As discussed in the Advisory Action mailed 5/27/2009, claim 4 of the 9/27/2007 claim amendment depended on a canceled claim (claim 3). As such claim 4 did not even recite any compound or disease. In such a situation, a proper rejection is that the subject matter of the claim was unclear; accordingly the claim was rejected under 35 USC 112, 2nd paragraph as indefinite. Inclusion of claim 4 in any specific prior art rejection was considered improper, since there was no step recited involving any compound or disease or patient population limitations. The fact that the claim was not included in the prior art rejection was not related to the patentability of the claim over the prior art; but that the subject matter was unclear. Applicant was clearly informed that the claim subject matter was indefinite (see p. 2, Item 4 of the 4/1/2008 Office Action).

Applicant argues some points about what would have occurred "if" the claim had been corrected, and that such a rejection would have been a new rejection basis, that should not have been made final. It is unclear what purpose this argument serves. Such a scenario is not the case.

The finality of the 1/12/2009 Office Action has been withdrawn based on the proper filing of a request for continued examination.

3. Applicant's arguments with respect to the rejection under 35 USC 112, 1st paragraph have been fully considered but they are only persuasive in part:

Claims 10, 2, 5, 7 and 11 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for treating pulmonary hypertension in

the sense of the meaning of reduction of pulmonary hypertension in individuals with pulmonary hypertension, does not reasonably provide enablement for treating individuals in the sense of the meaning of prophylactic treatment.

With respect to new claim 11 (and amended claim 10), the prevention embodiment is present within the meaning of treating recited in independent claim 10 and all claims dependent thereon. The rejection of record is therefore also applicable to claim 11.

Applicant argues that the examiner states the specification is enabling for curative treatment, but not for prophylactic treatment; but the examiner has provided no scientific rationale to explain why a compound which has efficacy for treating ongoing episodes of the condition would not also prevent the onset or recurrence of the condition. To clarify the record, curative treatment with the traditional meaning of completely getting rid of the ailment is not considered enabled. Only when the term "curative" is taken with the meaning of "having efficacy with respect to episodes of pulmonary hypertension"; i.e., a reduction in hypertension levels, falling within the scope of claim 10, is this definition of “curative treatment” considered enabled. Therefore, only when given this specific meaning is curative considered enabled, but if curative were to be construed to have the more usual meaning in the art of completely alleviating pulmonary hypertension, this alternate definition of curative treatment would not be enabled. Reducing levels of pulmonary hypertension is not identical to the complete removal of pulmonary hypertension (which would be required by the usual definition of "cure").

In contrast, "prevent" has the meaning of "to keep from happening or existing" (Merriam-Webster online definition of Prevent; http://www.merriam-webster.com/dictionary/prevent; accessed 10/14/2009). Therefore, the broadest reasonable definition for the prevention of the onset or recurrence of pulmonary hypertension embodiments within "treatment" implies that the condition will not occur upon the administration of the elected compound, irrespective of the cause of the pulmonary hypertension processes. The argument that no scientific rationale has been provided is not persuasive; such rationale was laid out in the Office Action of 4/1/2008; which clearly discussed that the state of the art indicates that PAH is a disease with poor prognosis, with a precise mechanism that still remains to be elucidated. While some drugs are currently used in treatment, more effective treatment still needs to be developed; unknown triggers contribute to the development of pulmonary hypertension. Taken with the data of the specification, where 80% reduction in levels of pulmonary hypertension in rats has been disclosed, this supports reducing the pulmonary blood pressure levels, but neither the complete removal of the disease nor prevention of the disease is demonstrated, nor is persuasive rationale presented leading to the extrapolation of reducing pulmonary blood pressure to keeping pulmonary hypertension from occurring. Prevention requires more than just a partial reduction in pulmonary arterial blood pressure levels; it requires that the condition will not develop as a result of the administration of the claimed drug, even in the presence of known or unknown disease triggers that would normally lead to the development of the disease. Therefore,

the embodiment within the claims of prevention is still considered to require undue experimentation to practice the invention, for which the rejection is maintained.

4. Applicant's arguments with respect to the rejection under 35 USC 103 have been fully considered but they are not persuasive:

Claims 10, 2, 5, 7 and 11 are rejected under 35 U.S.C. 103(a) as being unpatentable over Goncharova, et al. ("PI3K is required for proliferation and migration of human pulmonary vascular smooth muscle cells"; 2002 Mar 8; Am. J. Physiol. Lung Cell. Mol. Physiol.; 283: L354-L363; cited in a prior Office Action); Tanabe, et al. ("Mechanical stretch augments PDGF receptor β expression and protein tyrosine phosphorylation in pulmonary artery tissue and smooth muscle cells"; 2000; Molecular and Cellular Biochemistry; 215: 103-113; cited in a prior Office Action); Zimmermann, et al. (WO 99/03854 A1; 1999; IDS 4/21/2005 reference AM); and Dingli, et al. ("Unexplained Pulmonary Hypertension in Chronic Myeloproliferative Disorders"; 2001; Chest; 120 (3): 801-808; cited in a prior Office Action).

It is noted that claim 10 has been amended to remove the requirement for a 3 month time period, and this limitation has been introduced into new claim 11, dependent on claim 10. Since the rejection of record already addressed the claim 11 limitation, this embodiment would also be within the scope of claim 10.

Applicant argues that: 1) the references do not implicate PDGRF in pulmonary hypertension, but merely report on pathways involving PDGFR activity may be related to pulmonary hypertension or that PDGFR is overexpressed in PH, but neither suggests PDGFR inhibition as a therapy to control PH. This is not persuasive; as present on the

record, Goncharova indicates that targeting PI3K-dependent human PVSM cell motility and proliferation may offer a potential target in blocking development of hypertension (p. L362, last paragraph); the references imply the relationship that exists between PDGFR activity and pulmonary hypertension would lead to the expectation that reduction of such activity (i.e., by inhibition of PDGFR) would reduce the contribution of this pathway to pulmonary hypertension.

Applicant further argues: 2) Goncharova does not teach that imatinib inhibits cell proliferation and motility, but rapamycin has these properties; that Goncharova teaches S6K1 plays a potentially important role in PSVM cell mitogenesis and that PVSM cell proliferation demonstrates high sensitivity to rapamycin, a specific inhibitor of S6K1; i.e., Goncharova leads the skilled artisan to take a different approach. The fact that, for example, Goncharova teaches cell proliferation and motility is a critical step in vascular remodeling (important in diseases including pulmonary hypertension), coupled with Zimmerman, which teaches diseases with vascular smooth-muscle cell migration and proliferation where PDGR and PDGF-R often play a role, such as restenosis and artherosclerosis (Zimmerman, p. 17, 1st paragraph), is an indication that both rapamycin and imatinib have the same art recognized properties of inhibition of cell migration and proliferation, which play important roles in progression of pulmonary hypertension. Therefore it would have been obvious to utilize imatinib in treating pulmonary hypertension. Applicant is referred to MPEP 2144.06 (II), which indicates it would be obvious to substitute equivalents known for the same purpose (imatinib for rapamycin, both with cell migration and proliferation inhibiting activity, in this case).

Applicant additionally argues: 3) Tanabe describes experiments which suggest that PDGFR may play a role in vasulature hypertensive diseases, but does not reach the conclusion that inhibiting PDGFR may provide a therapeutic benefit for such diseases; that Tanabe describes experiments that lead to the conclusion that stretch triggers the overexpression of PDGFRbeta in vasculature hypertensive diseases; thus PDGFR system may play a significant role in the development of several hypertensive diseases. This report is only a report of experiments that suggest a correlation between PDGF-Rbeta and vasculature hypertensive diseases, such as pulmonary hypertension, but does not suggest that the inhibition of PDGFR as an appropriate treatment for the condition. One of ordinary skill in the art would have had the expectation that inhibiting PDGFR would lead to the reduction of the extent of pulmonary hypertension disease process based on the correlations of Tanabe, in part, and for the reasons of record: 1) both Goncharova and Tanabe implicate the role of PDGF-R in pulmonary hypertension and Zimmerman teaches imatinib is useful in diseases where PDGF-R plays a role; 2) Gocharova teaches cell proliferation and motility is a critical step in vascular remodeling, imatinib inhibits such processes; and 3) Tanabe teaches phosphorylation of PDGF receptor β by stretch in endothelial cells is a component of pulmonary hypertension, such phosphorylation is inhibited by imatinib. These points, when taken together, lead to a reasonable expectation of success in reducing the progress of the disease, i.e., in treating pulmonary hypertension by administration of imatinib.

Applicant further argues that the references do no more than suggest a connection between PDGFR and pulmonary hypertension; which is merely an invitation

to experiment which provides no basis to have a reasonable expectation that PDGFR inhibition would be useful for the treatment of pulmonary hypertension; that the combined disclosure would not lead to the present invention, but to experiment with S6K1 inhibitors like rapamycin, not PDGFR inhibitors. The connection between PDGFR and pulmonary hypertension that has been established would lead to a reasonable expectation of reducing the effect of high levels of PDGFR activity, a condition that is associated with pulmonary hypertension, and the detrimental effects of, for example vascular remodeling, and the stretch induced phosphorylation processes. Both of these lead to the expectation of a benefit in treatment of pulmonary hypertension disease progression. With respect to rapamycin, this argument has been addressed above.

Conclusion

5. No claim is allowed.

6. Any inquiry concerning this communication or earlier communications from the examiner should be directed to TIMOTHY P. THOMAS whose telephone number is (571)272-8994. The examiner can normally be reached on Monday-Thursday 6:30 a.m. - 5:00 p.m..

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Brandon Fetterolf can be reached on (571) 272-2919. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Timothy P Thomas/
Examiner, Art Unit 1628